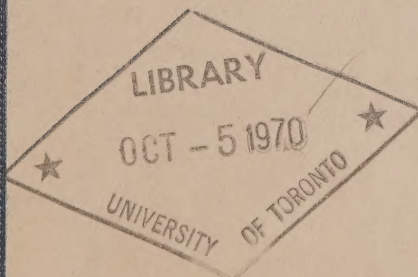
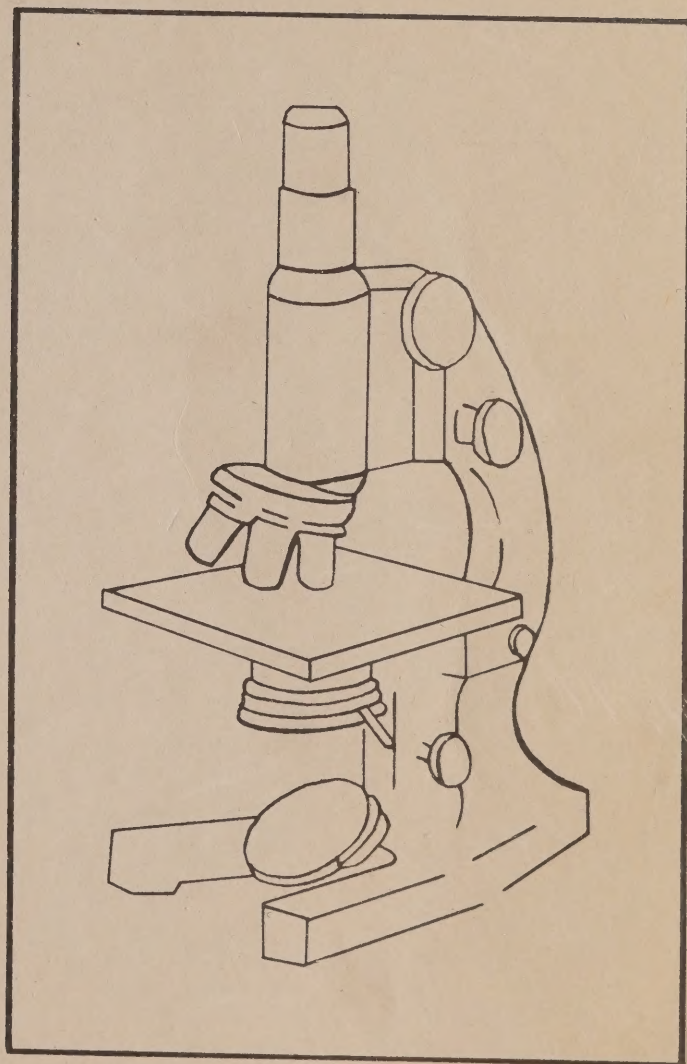


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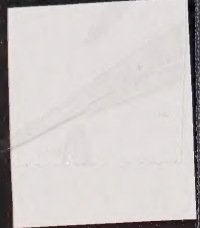
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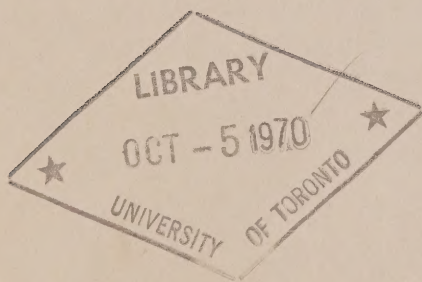
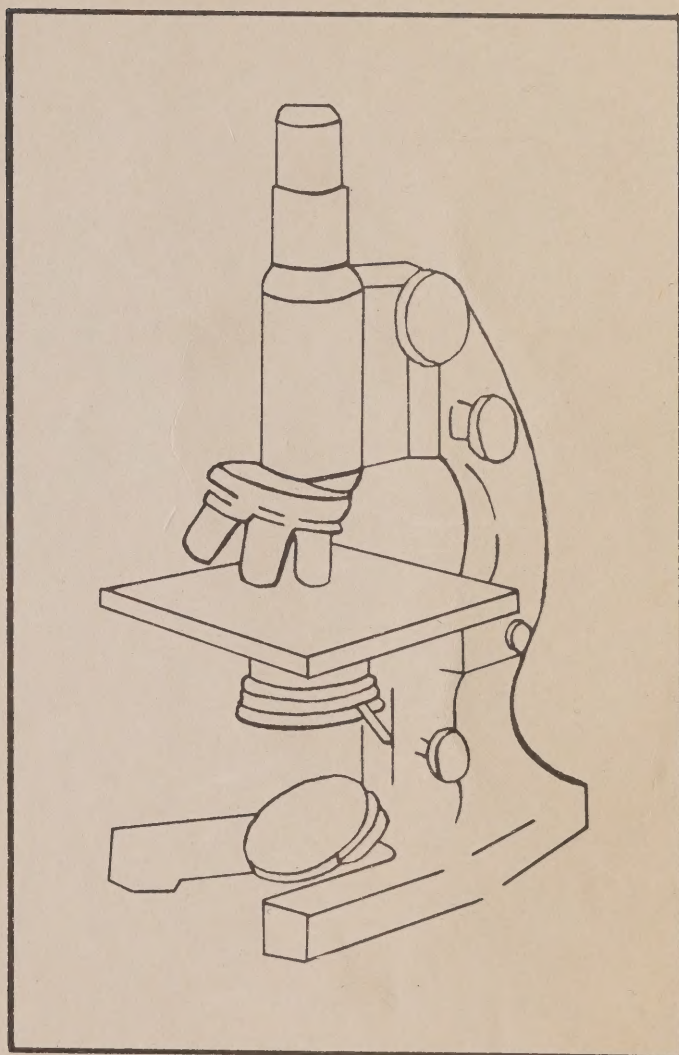
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FOOD AND DRUG DIRECTORATE

RESEARCH LABORATORIES

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RESEARCH LABORATORIES

Food and Drug Directorate
Ottawa – Canada

The Food and Drug Directorate of the Department of National Health and Welfare is responsible for the administration and enforcement of the Food and Drugs Act, the Proprietary or Patent Medicine Act and the Narcotic Control Act. These three acts are designed to protect consumers from health hazards and fraud or deception in the manufacture, labelling, advertising and sale of foods, drugs, cosmetics and medical devices.

The Research Laboratories of the Directorate located in Ottawa, employ nearly 250 scientists and support staff in the conduct of research in such diverse fields as food chemistry, pharmaceutical chemistry, pharmacology, endocrinology, nutrition, microbiology, pathology and toxicology. It brings together highly trained scientists, many of whom are recognized internationally, with specialization in disciplines such as biochemistry, physical, organic and analytical chemistry, pharmacy, physiology, pharmacology, and pathology. Scientists are encouraged in all aspects of professional development, including attendance at scientific meetings, publication of results, and educational leave.

The programme of the Laboratories, as summarized in the following pages, is related to the broad regulatory needs of the Directorate. The results of research work during the past year (1968) have been published in about 110 articles in the scientific literature. The various Research Divisions collaborate with workers in other institutions in many parts of the world and take an active part in organizations such as the World Health Organization, Food and Agriculture Organization, Association of Official Analytical Chemists and International Standardization Organization. In addition, the Laboratories serve as a training ground for scientists from many parts of the world who are sponsored by W. H. O., Colombo Plan, and the National Research Council Post-Doctorate Fellowship Program.

The Research Laboratories are organized into five Divisions (Food, Microbiology, Nutrition, Pharmaceutical Chemistry, Pharmacology) a Laboratory Animal Medicine Section, a Scientific Services Section and service units (Animal Care, electronic services, and glassblowing); trained technical assistants are available to work with professional workers. To cope with the rapid development in the food and drug fields, plans have been made for a new building to provide the most modern laboratory and animal facilities, which will accommodate more than double the present staff and be completed by late 1972.

W.P. McKinley
Acting Director, Research Laboratories



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PHARMACOLOGY DIVISION

Dr. A.J. Liston, Acting Chief

The Pharmacology Division is responsible for research on the safety and efficacy of chemicals affecting living protoplasm, including drugs, hormones, food additives and cosmetics. The area of investigation is extremely broad, including the fields of biochemistry, endocrinology, pathology, toxicology and pharmacology. A wide variety of biological and chemical procedures are used, ranging from clinical assessment of the effects of drugs on animals to highly sophisticated biochemical procedures for evaluation of drug metabolism by isolated enzyme systems. Because of the great importance to public health of increased knowledge concerning biological effects of drugs, hormones, pesticides and other chemicals, considerable expansion in the staff of the Division is anticipated during the next few years.

Biochemistry

This section is concerned with investigations on the absorption, distribution, biotransformation and excretion of drugs and other foreign substances which affect living protoplasm. The studies involve the identification and quantitative determination of the products of drug metabolism in the urine and plasma of experimental animals and of human subjects, as well as *in vitro* investigations of drug-metabolizing enzymes in liver microsomes. Other areas of current interest include studies on purine, pyrimidine and nucleic acid metabolism, and molecular transformations involved in the *in vivo* production of carcinogenic compounds.

Endocrinology

The Endocrinology Section is responsible for the investigation of the chemical and biological properties of endocrine products such as sex hormones, adrenocortical steroids, gonadotrophins, corticotrophin, growth hormone, insulin and thyroid hormones. Currently, work is proceeding on the elucidation of the relationship between biological activity and molecular structure of human gonadotrophins and of adrenocortical steroids. Synthesis of peptides is also being carried out relating to the examination of the regions of activity in the molecule of protein hormones. Other programs include a study of alterations in the *in vitro* hepatic detoxification of estrogens in connection with the active site of contraceptive steroids and an investigation of the effect of nutritional deficiencies on the metabolism of hormonal steroids. A project to examine the possible interactions between drugs affecting the C.N.S. and endocrine products has been initiated. The section is also engaged in evaluating the therapeutic effectiveness of certain insulin preparations.

Pharmacology

The research program of this section includes investigation of the effects of drugs at both molecular and physiological levels with particular emphasis on studies of mechanism of action and drug interactions. The fundamental physico-chemical aspects of drug transfer across membranes are being investigated to determine the feasibility of using a monolayer of living cells to estimate the kinetics of *in vivo* diffusion processes in an *in vitro* controllable environment; the factors involved in membrane transport of drugs where

diffusion limits availability can then be determined precisely. Animal models have been developed which permit measurement of placental transfer of drugs in both directions, metabolism of drugs by the foetus and assessment of the pharmacodynamic effect of drugs on the foetal cardiovascular system. The development of drug metabolism activity in the foetus and new born animal is being assessed using *in vitro* enzyme systems and liver perfusion techniques. Work is beginning in the area of the pharmacodynamics of some drug interactions.

Immunology

Studies have been initiated on the development of *in vitro* assays designed to predict allergic reactions in man to a variety of drug and food allergens. Preliminary results indicate that exposure of blood leucocytes from penicillin-allergic individuals to penicillin results in release of histamine from these cells. Furthermore, these results are more consistent with individuals who have had recent reactions compared to those having reactions two or more years ago.

A model system which serves to study the participation of serum antibodies in these allergic reactions is being developed. For this purpose, peritoneal rat mast cell degranulation and histamine release from human skin is being observed during antigen-antibody reactions.

Pathology and Toxicology

This section is responsible for investigation of pathologic and toxicologic changes that occur in animals and man as a result of treatment with additives and cosmetics. A multi-disciplinary approach is employed which utilizes the specialized skills of pathology, veterinary, medicine, biochemistry, physiology, and pharmacology, and includes clinical diagnosis, gross pathology, histology, histochemistry, hematology, clinical biochemistry, enzymology, electron microscopy, embryonal toxicology, drug metabolism, and the more classical techniques of acute and chronic toxicity testing.

Investigations are now in process on modifying factors in carcinogenesis, toxic and teratogenic effects of chemicals on animal embryos, effect of drugs on male rat fertility, early detection of drug toxicity by measurement of altered thyroid function, effects of alcohol on drug toxicity, food toxicology, carcinogenic potential of placentally transferred fungal toxins, effects of drugs on chromosomes, toxicity and metabolism of artificial sweetness.

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FOOD DIVISION

Dr. E. Somers, Chief

FOOD DIVISION

The Food Division is concerned with the development of methods for the analysis of intentional and adventitious additives in foods together with contaminants of biological or metallic origin. A program on the chemical composition of foods, particularly with meat and fruit products, is designed to provide criteria of purity and quality. The scientists in the Food Division are drawn from a wide range of disciplines so that they can provide the expertise to orientate the programs on basic principles.

Pesticides

This section is responsible for research on pesticide chemicals including both analytical methodology and investigations of their biochemical effects. The programs are oriented to assist in the enforcement of the Food and Drugs Act in respect of pesticide residues in foodstuffs and to assure the safety of such residues in man. Current research projects include development of a general screening method with confirmation procedures for pesticide residues utilizing automated GLC analytical systems and a programmed computer. Enzyme inhibition techniques are being developed for the carbamate insecticides. A program to develop and maintain pesticide analytical reference standards for use in research and regulatory laboratories has been initiated. The metabolism of pesticides in soil, plants and animals is being investigated; studies include determination of metabolites formed, rates of depletion and factors affecting the transformations. Animal studies include biochemical and physiological investigations with particular emphasis on pesticide-nutrient interactions and events during the perinatal period. This research is currently being extended to humans using necropsy tissue.

Food Additives

Chemical compounds used as food additives range from simple inorganic salts to complex organic compounds; they are designed to act as emulsifiers, stabilizers, sweeteners, preservatives, flavours etc. Work in this section is currently devoted to the development of methods for the analysis of several of these additives and their metabolites in food and animal systems.

Food Contaminants

This section is concerned with biological and metal contaminants of foodstuffs and with development of methods for their detection and measurements. Current research is devoted to the investigations on chemical properties and structure of new toxins isolated from fungi, and on the development of sensitive methods for their detection in foods. Work is in progress on the development of specific chemical methods for the detection of fungi, insects, mites and bacteria in foods.

Methods have been developed for the determination of nitrosamines in foods and body fluids. The isolation and characterization of unknown nitrosamines in foods, and

the formation of these compounds in human stomach, from nitrite and secondary amines, are being investigated. Studies on other naturally occurring carcinogenic and toxic compounds in foods are planned.

The levels of traces of heavy metals in foods are determined by atomic absorption spectrophotometry and X-ray fluorescence spectroscopy and a wide variety of foods have been surveyed.

Food Composition

This section studies the chemical composition of foods and develops methods to detect and measure food adulteration. Work is in progress on the protein composition of meat products and on methods to determine the source and amount of specific meat and non-meat proteins in cooked and uncooked meat products. Particular attention is being given to the immunological detection and measurement of heat stable proteins such as glycinin and glycoproteins. A method has been developed for the immunological determination of the soya protein content of meat products. Research is in progress on the composition of fruit juices, jams and jellies with particular emphasis on the distribution of phenolic compounds in these products. Methods are being developed for the identification and determination of purity of citrus fruit juices.

Research will be initiated shortly on the development of methods for the detection and measurement of drug residues in foods of animal origin.

Analytical

This group is concerned with the evaluation and modification of methods for food analyses, surveys and collaborative studies and routine food analyses. Current projects include a national survey of organochlorine insecticide residues in human fat, food colour certification, and collaborative studies on the analysis of aflatoxin and other mycotoxins.

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..... J.C. Meranger and E. Somers.
Analyst 93, 799-801, 1968.

Correlation of the Levels of Several Constituents of Commercial Orange Juices.

..... D.E. Coffin.
J.A.O.A.C. 51, 1199-1203, 1968.

TLC-Enzyme Inhibition Procedure to Detect Some Carbamate Standards and Carbaryl in Food Extracts.

..... P.J. Wales, H.A. McLeod, and W.P. McKinley.
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The Relative Sensitivity of Various Reagents for the Detection and Differentiation of Sugars and Sugar Derivatives in Glycoproteins.

..... Jos. Mes. and L. Kamm.
J. Chromatog, 28, 120-125, 1968.

Physico-Chemical and Biophysical Factors Affecting the Activity of Pesticides. Transport and Accumulation of Fungicides by Fungal Conidia.

..... E. Somers.
S.C.I. Monograph 29, London, 243-250, 1968.

Simplified Method of Preparing Column Materials for Gas-Liquid Chromatographic Separation of Some Pesticides.

..... C.E. Mendoza, K.A. McCully, and P.J. Wales.
Anal. Chem. 40, 2225-227, 1968.

On the Spectrophotofluorometric Determination of Nanogram Amounts of Diaminopimelic Acid, a Bacterial Cell Wall Constituent.

..... N.P. Sen, E. Somers and R.C. O'Brien.
Anal. Biochem. 26, 457-458, 1968.



PHARMACEUTICAL CHEMISTRY DIVISION

Dr. Denys Cook, Chief

The research activities of the Pharmaceutical Chemistry Division are directed towards a better understanding of the chemistry including physical chemistry of drugs both as pure chemical substances, and as the finished pharmaceutical products available to the consumer. These research studies also embrace the chemistry of drugs and drug dosage forms *in vivo* in humans and animals.

The Division advises the Directorate on aspects of pharmaceutical chemistry relating to drug manufacture, processing and quality control. It also participates in collaborative studies with pharmacopoeial commissions and assists international agencies in the establishment of drug standards and specifications.

Analytical Chemistry Section

Research into the chemistry of pure drug substances permits both qualitative and quantitative techniques for their identification and assay, and leads confidently to methods of analysis of the drug in dosage form. The stability of drugs in different environments is an important part of this work, and sophisticated procedures for separation, identification and assay of degradation products are being devised. The use of automated equipment in drug analysis is increasing in importance.

Biopharmaceutics Section

Variation in formulation of a drug into a finished dosage form may affect the blood level and excretion pattern of a circulating drug and metabolites. Studies in man are carried out on the bio-availability of different manufactured dosage forms, which is preceded by the establishment of rigorous techniques for the identification and measurement of drug and metabolites in blood and urine. Pharmacokinetic aspects of circulation and excretion are an intrinsic part of these studies.

The effect of concomitant administration of one or more additional drugs, is determined as well as such influences as meals, sleep, exercise and other physiological factors.

In vitro models of drug transfer, dissolution, complex formation, and partitioning are studied and are helpful in the task of establishing laboratory markers of drug availability.

Natural Products Section

This section is responsible for the examination of drugs of natural origin, including antibiotics and formulations covered by the Proprietary or Patent Medicine Act. Crude drugs are being studied to provide methods applicable to the control of such medicines. When new constituents are found in these products, attempts are made to isolate and purify them so that their pharmacological activity and chemical structure can be

studied. The active principles in toxic plants are being examined. Chemical and physico-chemical techniques are being used in the study of antibiotics. Drugs of abuse, including narcotics and psychotomimetics are being characterized and methods devised for the assay of medicinal preparations covered by the Narcotic Control Act.

Recent Publications

Thin-Layer Chromatographic Identification of Thirteen Medicinally Important Carbamates.

..... T. W. McConnel Davis
J. Chromatog. 29, 283, (1967).

The Isolation and Structure of Papaverrubin C (Epiporphyroxine).

..... D. W. Hughes, L. Kuhn and S. Pfeifer.
J. Chem. Soc. C. 444 (1967).

Determination of Phosphate in Tetracycline Preparations.

..... H. D. Beckstead, W. N. French and J. F. Truelove.
Can. J. Pharm. Sci. 2, 9 (1967).

Detection and Separation of Penicillins by Thin-Layer Chromatography

..... I. J. McGilveray and R. D. Strickland.
J. Pharm. Sci. 56, 77 (1967).

Improved Method of Assay of Pyrvinium Pamoate and Its Official Preparations.

..... H. D. Beckstead and S. J. Smith
J. Pharm. Sci. 56, 390 (1967).

Pharmaceutical Controls for Drug Availability.

..... D. Cook
Med. Serv. J. 23, 323 (1967).

Quality Assurance in Proprietary Medicine.

..... D. W. Hughes.
Med. Serv. J. Canada 23, 287 (1967).

Stability of Drugs and Drug Products.

..... W.N. French.
Med. Serv. J. Canada 23, 308 (1967).

Selection of Raw Materials.

..... I. J. McGilveray.
Med. Serv. J. Canada 23, 283, (1967).

Response of Two Species of Ipomoea to Gibberellic Acid Treatment.

..... K. Genest
Lloydia 30, 164 (1967).

Physico-Chemical Characterisation of Some 5,5-Disubstituted-1,3-Dioxanthyl Barbituric Acids.

..... B. C. Flann and J. A. R. Cloutier.
Applied Spectroscopy 21, 225 (1967).

Essential Oils and Their Constituents. XXXIV. Isolation of Khusenin Acid from Oil of Vetiver and Some Observations Concerning Their Structures.

..... I. C. Nigam and H. Komae.
J. Pharm. Sci. 56, 1299 (1967).

The Infrared Spectra of Caffeine Salts

..... D. Cook and Z. R. Regnier.
Can. J. Chem. 45, 2895 (1967).

The Infrared Spectra of Theobromine Salts.

..... D. Cook and Z. R. Regnier.
Can. J. Chem. 45, 2899 (1967).

Thin-Layer Chromatographic Acids.

..... H. D. Beckstead, W. N. French and S. J. Smith.
J. Chromatog. 31, 226 (1967).

Reaction Gas Chromatography III.

..... C. Radecka and I. C. Nigam.
J. Pharm. Sci. 56, 1608 (1967).

The Determination of Laudanine in Opium by Direct Densitometric Thin-Layer Chromatography.

..... K. Genest and G. Belec.
Can. J. Pharm. Sci. 2, 44 (1967).

Pharmacopeial Standards and Specifications for Bulk Drugs and Solid Oral Dosage Forms.

..... W. N. French, F. Matsui, D. Cook and L. Levi.
J. Pharm. Sci. 56, 1622 (1967).

Essential Oils and Their Constituents. Part XXXVI. X-Ray Powder Diffraction Data for Semicarbazones of Aldehydes and Ketones.

..... J.C. Meranger, J. C. Bartlett, C. Radecka and I. C. Nigam
Perf. and Essential Oil Rec. Oct. (1967).

Colorimetric Analysis of Imipramine, Desipramine and Trimipramine by a Nitrous Acid Procedure and by the Acid Dye Technique.

..... W. N. French, F. Matsui and J. F. Truelove.
Can. J. Pharm. Sci. 3, 33 (1968).

Selective Determination of Tolbutamide in Pharmaceutical Dosage Forms by Reaction with Ninhydrin.

..... K. K. Kaistha and W.N. French.
J. Pharm. Sci. 57, 459 (1968).

Colorimetric Assay and Improved Method for Identification of Vancomycin Hydrochloride.

..... J. R. Fooks, I. J. McGilveray and R. D. Strickland.
J. Pharm. Sci. 57, 314 (1968).

Determination and Thin-Layer Chromatography of Phenylbutazone in the Presence of Decomposition Products.

..... H. D. Beckstead, K. K. Kaistha and S. J. Smith
J. Pharm. Sci. 57, 1952 (1968).

Muscarine in *Clitocybe* Species.

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J. Pharm. Sci. 57, 331 (1968).

Potentiation of Ethanol by *Coprinus Atramentarius* in Mice.

..... K. Genest, B. B. Coldwell, and D.W. Hughes.
J. Pharm. Pharmacol. 20, 102 (1968).

Alkaloids of *Peumus Boldus*. Isolation of (+) reticuline and isoboldine.

..... D. W. Hughes, K. Genest and W. Skakum.
J. Pharm. Sci. 57, 1023 (1968).

Chromatographic Methods for the Identification of the New Hallucinogen, 4-methyl-2,5-dimethoxy- α -methylphenethylamine (STP) and related drugs.

..... K. Genest and D. W. Hughes.
The Analyst 93, 485 (1968).

Alkaloids of *Peumus Boldus*. Isolation and Laurotetanine and Laurolitsine.

..... D. W. Hughes, K. Genest and W. Skakum.
J. Pharm. Sci. 57, 1619 (1968).

Natural Products in Canadian Pharmaceuticals, I. Alkaloids. Methods of Identification.

..... K. Genest and D. W. Hughes
Can. J. Pharm. Sci. 3, 77 (1968).

Natural Products in Canadian Pharmaceuticals, II. *Peumus Boldus*.

..... K. Genest and D. W. Hughes
Can. J. Pharm. Sci. 3, 84 (1968).

Identification of Ketones in Cyperus: NMR and Mass Spectral Examination of the 2,4-Dinitrophenylhydrazones.

..... G. A. Neville, I. C. Nigam and J. L. Holmes.
Tetrahedron 24, 3891 (1968).

Identification of Sesquiterpene Hydrocarbons in Oil of Opoponax.

..... I. C. Nigam and G. A. Neville.
J. Chromatog. 34, 85 (1968).

Structural Relationships Between Tricyclic Sesquiterpenes in Oils of Vetiver.

..... I. C. Nigam, H. Komae, G. A. Neville, C. Radecks and S. K. Paknikar.
Tetrahedron Letters, 2497 (1968).

The Metabolism of Hydroxyskatoles in the Rat.

..... G. L. Mattock, M. E. Mahon and A. Hoffer.
Biochem. Pharmacol. 17, 1425 (1968).

Steroid Hormone Analogs. IV. C-Nor-D-homoestrone.

..... S. M. Kupchan, A. By and M. S. Flom
J. Org. Chem. 33, 911 (1968).

Steroid Alkaloids: The Veratrum Group.

..... S. M. Kupchan and A. W. By
In "The Alkaloids", (R.H.F. Manske, Ed.), Vol. X, Academic Press Inc., New York, pp 193 (1968).

Essential Oils and Their Constituents XIII. Isomerization of Epoxides on Active Alumina.

..... I. C. Nigam and L. Levi.
Can. J. Chem. 46, 1944 (1968).

Essential Oils and Their Constituents. XXXIX. Structures of Khusenic Acid and Isokhusenic Acid Two Sesquiterpenic Constituents of Oil of Vetiver.

..... H. Komae and I. C. Nigam.
J. Org. Chem. 33, 1771 (1968).

Detection of Impurities in Medicinal 1,4-Benzodiazepines and Related Compounds by Thin-Layer Chromatography.

..... H. D. Beckstead and S. J. Smith
Arzneimittel-Forschung 18, 529 (1968).

Perspectives in the Growth of Chemical Knowledge. I. The Discovery of Gases.

..... G. A. Neville

Can. Chem. Ed. 4, 14 (1968).

Isolation and Concentration of Traces of Lead with Strontium Sulfate.

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J.A.O.A.C. 51, 719 (1968).

A Sintered Glass Filter Funnel for Compressed Tablet Dissolution Rate Studies.

..... D. Cook

Can. J. Pharm. Sci. 2, 91 (1968).

The Kostanecki-Robinson Acylation and Cyclisation of 3-Acyl- α -Hydroxy-2-Pyromes.

..... D. Cook and J. S. McIntyre.

J. Org. Chem. 33, 1746 (1968).

Complexes of N.-Methylxanthines with Carboxylic Acids.

..... D. Cook and Z. R. Regnier

Can. J. Chem. 46, 3055 (1968).

Gas Chromatographic Analysis of Rose Oils of Different Geographical and Botanical Origins.

..... I. C. Nigam and C. Radecka.

ISO Bulletin 20, 261 (1968).

The Physiological Availability and In Vitro Dissolution Characteristics of Some Solid Dosage Formulations of Para-amino Salicylic Acid and Its Salts.

..... E. J. Middleton, H. S. Chang and D. Cook.

Can. J. Pharm. Sci. 3, 97 (1968).



MICROBIOLOGY DIVISION

Dr. H. Pivnick, Acting Chief

The Microbiology Division engages in research on the microbiology of foods, with the chief responsibility to provide the Directorate with the experimental facts necessary to establish the existence and extent of disease hazard and to make sound proposals for protection of consumers from food-borne disease of microbial origin. In this area every effort is made to anticipate potential public health problems of a microbial nature, whether arising from changing industrial practices, pollution, or newly recognized through the understanding given by fundamental scientific developments. The area of investigation is therefore broad in scope. Current studies embrace the bacterial food-borne pathogens, with special reference to hazardous species to be anticipated from other parts of the world, the food-poisoning toxins, mycotoxins, microbial biochemistry, cytology, microbial ecology, taxonomy, irradiation microbiology and microbiological methods. Close collaboration has been maintained with FAO/WHO Expert Committees and other international and national organizations in these various areas of food microbiology.

Bacterial Toxins

Investigation of food-borne toxins and specific endotoxins of aerobic and anaerobic food-borne bacteria includes: fractionation of filtrates of toxinogenic cultures; amino-acid composition and structure of purified toxins; assay procedures – animal tests, haemagglutination, immunochemical, isotope dilution procedures; determinative methods; toxin precursors and the cellular site of formation; nutritional requirements. The ligated loop technique has been developed for study of the cause of food-poisoning by *Clostridium perfringens* and *Vibrio parahaemolyticus*. The molecular weights of the haemagglutinins and neurotoxic moieties of the botulism toxins have been determined, and sensitive extractive procedures have been developed. The diversity of the Staphylococcal enterotoxins is under study.

Mycotoxins

Current research interest in fungal toxins includes: determination of optimal media and environmental conditions for production of the lesser-known and new mycotoxins; potential bioassay systems, including test-animals and tissue-culture; foods allowing the production of specific mycotoxins; a survey of food-borne fungi for mycotoxinogenesis; toxinogenic fungi in foods associated with otherwise nondiagnosed illnesses; collaboration in estimation of carcinogenesis by mycotoxins.

Microbial Ecology

This group is concerned with the microbial ecology of foods as influenced by new or modified processing treatments, the use of antibiotics or other food additives, storage and packaging processes, etc., with special reference to multiplication of pathogens and toxin formation. Current experimental interest includes: factors influencing the production of botulinal toxins in processed foods; the effect of curing salts on spore outgrowth and toxin formation of *Cl. botulinum*; the mode of action of nitrite in restriction

of spore germination; food-poisoning from barbecued chicken and the effect of common spoilage organisms on toxin development; *Salmonella*-coliform interactions. A collection of spoilage organisms is being developed for later comparative taxonomy where a group is shown to have a particular role.

Irradiation Microbiology

The essential purpose here is the exploration of microbiological hazards that might arise through the selective and mutagenic activities of gamma irradiation when used in food preservation. Much of the Division's biochemical potential is applied to the specific fundamental studies prerequisite to reaching a safe judgement on this highly complex problem.

Irradiation-induced mutants of food-borne bacteria are being examined biochemically in order to provide understanding of the basis for irradiation resistance. Currently under study, using susceptible and resistant strains, are the extent of degradation of DNA, both single-strand and double strand breaks; rates of DNA repair, enzymes involved in repair and replication of DNA; mesosome formation in relation to resistance and the multigenomic state; enzymic systems involved in observed repression and derepression of nucleotide synthesis; comparative electron microscope studies in relation to irradiation resistance; examination for new toxins from mutant-organisms.

Studies with basic bacterial proteins

A new group has been formed to explore further the role of particular basic proteins in bacteria, with current reference to antibiotic and/or toxin synthesis; and cationic uptake. The nisinoid polypeptides and some staphylococcal toxins will be investigated in this light.

Oriental Food-borne pathogens

Because of the risk that food-borne pathogens at present rare or unknown in this country may find their way into Canada, through international commerce and travel and as a sequel to wars in Asia, studies have been initiated to develop methods of detection and recognition, in foods, of pathogens such as *Vibrio parahaemolyticus*, *Vibrio cholerae*, the EL ToR vibrio, *Pseudomonas pseudonallei*. The severity of the effects of introduction of some of these into Canada could be much heightened by prevailing pollution.

Food-borne viruses

Among the most important sources of enteric disease are the viruses, many of which may be food and water-borne. A start has been made in this long neglected field, and a survey will be made initially of the viruses contributed from sewage polluted waters, sewage contact being a primary cause for contamination of foods. The long-term objective is to detect and identify virus particles in foods when present in low numbers but in the presence of large numbers of bacteria.

Methodology and Analytical

The objectives of this group are to carry out comparative appraisal of existing methods for the microbial analysis of foods and to advise Regional analytical laboratories; to take part in international interlaboratory testing of methods in food microbiology; to devise new methods. Specific bacterial enzyme systems are being investigated with a view to developing improved selectivity of methods for isolation and enumeration of pathogens from foods. For example, analogues of lactose which release a toxic moiety when activated by beta-galactosidase, are being adapted to a method for isolation of *Salmonella* from foods severely contaminated with coliforms. Specific fluorescent antibody preparations and immuno-electrophoresis are being used in developing improved methods for detection of the various serotypes of *Cl. botulinum*. Radioactive tracer techniques will be adapted to assay of specific toxins.

Recent Publications

Experimental food poisoning with heat-susceptible *Clostridium perfringens* Type A.

..... A.H.W. Hauschild and F.S. Thatcher
J. Food Sci. 32, 467 (1967).

Variations in recovery of *Clostridium perfringens* on commercial sulfite-polymyxin-sulfadiazine (SPS) agar.

..... A.H.W. Hauschild, I.E. Erdman, R. Hilsheimer and F.S. Thatcher
J. Food Sci. 32, 469 (1967).

Acid resistance of infectivity of food-poisoning *Clostridium perfringens*.

..... A.H.W. Hauschild, R. Hilsheimer and F.S. Thatcher
Can. J. Microbiol. 13, 1041 (1967).

Experimental enteritis with food poisoning and classical strains of *Clostridium perfringens* type A in lambs.

..... A.H.W. Hauschild, L. Niilo and W.J. Dorward
J. Infect. Dis. 117, 379 (1967).

Selective inhibition of *Escherichia coli* in the presence of *Salmonella typhimurium* by Phenethyl β -D-Galactopyranoside.

..... M.A. Johnston and F.S. Thatcher
Appl. Microbiol. 15, 1223 (1967).

Preparation of ^{14}C -labeled tuberculin purified protein derivative.

..... S. Landi, H.R. Held, A.H.W. Hauschild and R. Hilsheimer
Appl. Microbiol. 15, 839 (1967).

Effect of sodium nitrite and temperature on toxinogenesis by *Clostridium botulinum* in perishable cooked meats vacuum-packed in air-impermeable plastic pouches.

..... H. Pivnick, L.J. Rubin, H.W. Barnett, H.R. Nordin, P.A. Ferguson and C.H. Perrin
Food Technol. 21, 100 (1967).

Formation of aflatoxins by *Aspergillus ostianus* Wehmer,

..... P.M. Scott, W. van Walbeek and J. Forgacs
Can. J. Microbiol. 15, 945 (1967).

Mycotoxins from food-borne fungi.

..... W. van Walbeek, P.M. Scott and F.S. Thatcher
Can. J. Microbiol. 14, 131 (1967).

Effect of p-fluorophenylalanine on radiation sensitivity in *Escherichia coli*.

..... N. Dickie, D.A. Dennis and F.S. Thatcher
Can. J. Microbiol. 14, 799 (1968).

Food poisoning *Clostridium perfringens*.

..... A.H.W. Hauschild
Ass. Food & Drug Off. U.S. 32, 135 (1968).

Experimental gas gangrene with food-poisoning *Clostridium perfringens* type A.

..... A.H.W. Hauschild and F.S. Thatcher
Can. J. Microbiol. 14, 705 (1968).

Heterogeneity of *Clostridium botulinum* type A toxin.

..... A.H.W. Hauschild and R. Hilsheimer
Can. J. Microbiol. 14, 805 (1968).

Clostridium perfringens type A infection of ligated intestinal loops in lambs.

..... A.H.W. Hauschild, L. Niilo and W.J. Dorward
Appl. Microbiol. 16, 1235 (1968).

Staphylococcus food poisoning from barbecued chicken.

..... H. Pivnick, T.R.B. Barr, I.E. Erdman and J.I. Pataki
Can. J. Pub. Health 59, 30 (1968).

Retailing of barbecued chickens — A Canadian Survey.

..... H. Pivnick, I.E. Erdman, G. Micklea, D. Connolly, A. Loit, R. Hill, A. Mak and M. Milling
Can. J. Pub. Health 59, 380 (1968).

Growth of food poisoning bacteria on barbecued chicken.

..... H. Pivnick, I.E. Erdman, S. Manzatuik and E. Pommier
J. Milk and Food Technol. *31*, 198 (1968).

Microbial problems in food safety with particular reference to *Clostridium botulinum*.

..... H. Pivnick and F. S. Thatcher
"The Safety of Foods". The Avi Publishing Co., Wesport, Conn. 121 (1968).

Nutritional requirements of *Escherichia coli* resistant to gamma irradiation.

..... H. Robern and F.S. Thatcher
Can. J. Microbiol. *14*, 711 (1968).

Effects of γ -irradiation on *Escherichia coli* wild type and its radiation-resistant mutants. I.
Post-irradiation Synthesis of DNA.

..... S. Stavric, N. Dickie and F.S. Thatcher
Int. J. Radiat. Biol. *14*, 403 (1968).

Effects of γ -irradiation on *Escherichia coli* wild type and its radiation-resistant mutants. II.
Post-irradiation degradation of DNA.

..... S. Stavric, N. Dickie and F.S. Thatcher
Int. J. Radiat. Biol. *14*, 411 (1968).

Microorganisms in Foods: Their significance and methods of enumeration.

..... F.S. Thatcher and D.S. Clark
University of Toronto Press, Toronto, Canada 234 pp. (1968).



NUTRITION DIVISION

Dr. T.K. Murray, Chief

The Nutrition Division is responsible for nutritional and metabolic studies on protein, fat, vitamins and minerals, and for the development of analytical methods for nutrients in foods and pharmaceuticals. A wide variety of chemical, biological and microbiological procedures are used.

Proteins

This section is investigating several aspects of protein nutrition, including efficacy and safety of amino acids used as food supplements or seasonings, and the relationship between protein nutrition and possible adverse effects of combinations of pesticides, food additives, and drugs. Methods used include blood and tissue analyses for protein, free amino acids, glucose, glycogen, cholesterol, urea, enzyme activity, and hormonal response.

Lipids

This group is studying the utilization and metabolism of lipids. Current work is centered on the determination of vitamin A status, the carotene content of food and its utilization, and the effect on phospholipid composition of various dietary alterations. The development of improved analytical methods are among the responsibilities of this group.

Minerals

The role of fluoride in osteoporotic bone loss is under investigation. It is also planned to study the availability of iron from its different forms used for fortification of wheat flour. Autopsy samples of human liver, spleen and bone marrow are being collected for the determination of iron stores.

Water-Soluble Vitamins

Research on all aspects of water-soluble vitamins is the responsibility of this group. Current work includes the development of automated methods for determining the vitamins in pharmaceutical products, foods and biological materials. This group has recently demonstrated that cigarette smokers had lower vitamin C levels than non-smokers and utilized their vitamin C intakes differently; research is continuing on this problem with the aim of determining the mechanism involved. The metabolism and antiscorbutic activity of D-isoascorbic acid (an antioxidant used by the food industry) is presently being investigated with guinea pigs and humans. Practical methods to evaluate the nutritional status of humans will be evaluated and wherever necessary new methods will be developed.

Recent Publications

Blood amino acid studies. VI. Use of plasma amino acid score for predicting limiting amino acid(s) in dietary proteins.

..... J.M. McLaughlan, S. Venkat Rao, F.J. Noel and A.B. Morrison
Can. J. Biochem. 45, 31, 1967.

Properties of the phospholipase B from penicillium natatum.

..... Joyce L. Beare and Morris Kates
Can. J. Biochem. *45*, 101, 1967.

The absorption and metabolism of anhydrovitamin A by the rat.

..... T.K. Murray and P. Erdody
Biochim. Biophys. Acta *136*, 375, 1967.

Interrelationship of vitamin A and C on tissue ubiquinones and sterols of rats and guinea pigs.

..... W.E.J. Phillips
Can. J. Biochem. *45*, 749, 1967.

Variation in polyunsaturates of special margarines.

..... Joyce L. Beare and Claudette Heroux and T.K. Murray
Can. Med. Assoc. J. *96*, 1575, 1967.

The B-oxidative degradation of docosenoic acids to eicosenic and octadenoic acids in the rat.

..... B.M. Craig and Joyce L. Beare
Can. J. Biochem. *45*, 1075, 1967.

Use of free plasma amino acid levels for estimating amino acid requirements of the growing rat.

..... J.M. McLaughlan and W.I. Illman
J. Nutr. *93*, 1, 1967.

Determination of ascorbic acid in enriched evaporated milk.

..... O. Pelletier
J.A.O.A.C. *50*, 817, 1967.

Effect of time factor on the nitrogen-sparing effect of dietary carbohydrate.

..... M. Narayana Rao and J.M. McLaughlan
Can. J. Biochem. *45*, 1653, 1967.

Effect of rapeseed oil on food intake in the rat.

..... Joyce L. Beare and John R. Beaton
Can. J. Phys. Pharm. *45*, 1093, 1967.

Lysin and methionine availability in heated casein-glucose mixtures.

..... M. Narayana Rao and J.M. McLaughlan
J.A.O.A.C. *50*, 704, 1967.

Effect of chlorophenoxyisobutyrate (CPIB) on rat liver non-saponifiables.

..... W.E.J. Phillips, M.R. Lakshmanan and R.L. Brien
Can. J. Phys. Pharm. *46*, 81, 1968.

Changes in the nitrate and nitrite contents of fresh and processed spinach during storage.

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Agric. Food Chem. J. *16*, 88, 1968.

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..... W.E.J. Phillips and R.L. Brien
Can. J. Biochem. *46*, 291, 1968.

Uptake of ³²P-orthophosphate and incorporation into phospholipids in tetrahymena pyriformis W exposed to phenothiazine derivatives.

..... C.G. Rogers
Can. J. Biochem. *46*, 331, 1968.

The *cis,cis*-linoleic acid content of heated oils.

..... Joyce L. Beare, B.P.C. Kennedy and C.M.A. Heroux
Can. Inst. Food Technol. J. *1*, 48, 1968.

Nutritional Properties of Canadian canbrea oil.

..... B.M. Craig and Joyce L. Beare
Can. Inst. Food Technol. J. *1*, 64, 1968.

Effect of p-chlorophenoxyisobutyrate (CPIB) fed to rats on hepatic biosynthesis and catabolism of ubiquinone.

..... M.R. Lakshmanan, W.E.J. Phillips and R.L. Brien
J. Lipid Res. *9*, 353, 1968.

Nitrate content of foods — Public Health Implications.

..... W.E.J. Phillips
J. Inst. Can. Technol. Aliment. *1*, 98, 1968.

Determination of vitamin D₂ and D₃ in pharmaceuticals by gas-liquid chromatography.

..... T.K. Murray, P. Erdody and T. Panalaks
J.A.O.A.C. *51*, 839, 1968.

Blood amino acid studies: Prediction of limiting amino acids in mixtures of dietary proteins.

..... S. Venkat Rao, F.J. Noel and J.M. McLaughlan
Can. J. Phys. Pharmac. *46*, 5, 1968.

Chemical determination of niacinamide in multivitamin preparations.

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J.A.O.A.C. 51, 4, 1968.

Survey of liver vitamin A stores of Canadians.

..... K. Hoppner, W.E.J. Phillips, T.K. Murray and J.S. Campbell
Can. Med. Assoc. J. 99, 983, 1968.

Utilization of carotene, vitamin A and triglyceride following oral intake of triton.

..... W.E.J. Phillips and R.L. Brien
J. Nutr. 96, 505, 1968.

Smoking and vitamin C levels in humans.

..... Omer Pelletier
Am. J. Clin. Nutr. 21, 1259, 1968.

Determination of vitamin C in serum, urine and other biological materials.

..... Omer Pelletier
J. Lab. Clin. Med. 72, 674, 1968.

Ubiquinone levels of human liver in health and disease.

..... W.E.J. Phillips, K. Hoppner, T.K. Murray and J.S. Campbell
Can. J. Phys. Pharmac. 47, 257, 1969.

Amino acids in blood plasma and tissues of rats following glucose force-feeding.

..... J.E. Knipfel, H.G. Botting, F.J. Noel and J.M. McLaughlan
Can. J. Biochem. 47, 323, 1969.

Liver phospholipids of rats deprived of dietary choline.

..... Joyce L. Beare-Rogers
Can. J. Biochem. 47, 257, 1969.

Differential determination of D-isoascorbic acid and L-ascorbic acid in quinea pig organs.

..... Omer Pelletier
Can. J. Biochem. 47, 449, 1969.

Vitamin A status and the metabolism of cholesterol in the rat.

..... M.R. Lakshmanan, W.E.J. Phillips and R.L. Brien
Br. J. Nutr. 23, 25, 1969.

Effect of inhibitors of cholesterol synthesis on rat liver ubiquinone.

..... W.E.J. Phillips and R.L. Brien
J. Atherosclerosis Res. 9, 113, 1969.

LABORATORY ANIMAL MEDICINE AND ANIMAL CARE UNIT

Animal Care Unit

Mr. W.J. Bellefeuille, Head

The Animal Care Unit provides and cares for the various species and strains of animals required for research projects conducted by the divisions of the Research Laboratories and other areas of the Directorate using experimental animals.

The Unit supplies caging, care and management for these animals and provides special diets. It works closely with researchers in providing the needed species, strains and management practices essential for specific experiments.

Laboratory Animal Medicine Section

Dr. H. Baer, Head

The Laboratory Animal Medicine Section, directed by a veterinarian, is responsible for the establishment and maintenance of a healthy animal colony. Diagnostic and investigational studies are conducted on the diseases and parasites affecting laboratory animals. Research is also conducted into environmental effects, (such as long-term isolation stress), on experimental animals. Advice and assistance is provided in experimental surgery projects and veterinary radiology.

Lectures and demonstrations are given to animal care personnel, technicians and researchers on all aspects of animal care and handling.

Recent publications:

Diplococcus pneumoniae type 16 in laboratory rats.

..... H. Baer

Can. J. Comp. Med. 31, 216, 1967.

RESEARCH LABORATORIES

FOOD AND DRUG DIRECTORATE

W.P. McKinley, B.Sc., M.Sc., Ph.D. (McGill) Acting Director

Barbara Summers B.A. (U. Western Ontario), Administrative Office

PHARMACOLOGY DIVISION

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S. Clayman, B.Sc. (Sir George Williams), Ph.D. (McGill)

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P. Toft, B.A., D. Phil. (Oxon)

D. Usher, B.Sc., M.Sc., Ph.D. (McGill)

H. Watanabe, B.Sc., M.Sc. (McGill)

Pathology and Toxicology

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 L. Trenholm, B.Sc. (Agr.) (McGill) Ph.D. (Cornell)
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 D. Stoltz, D.V.M. (University of Guelph)
 F. Iverson, B.S.A. (Ontario Agricultural College) Ph.D. (North Carolina State Univ.)

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 A. Cherrington, B.Sc. (U.N.B.)
 G.H. Hirsch, B. Pharm., M.Sc. (Alberta)
 J.D. Kohli, Dip. Med. (Punjab) M.Sc. (Chicago) Ph.D. (Manitoba)
 W. Schwark, D.V.M. (O.V.C.) M.Sc. (Guelph)
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 J. Withey, B.Sc., Ph.D. (University of London)
 L. Clark, B.S.P. (University of Saskatchewan) M.Sc. (Western)

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M. Nakano, B.Sc., M.Sc., Ph.D. (Univ. Wisconsin)

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K. Genest, Diplom-Chemiker (Berlin)

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Experimental Animal Medicine Section

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